

REMARKS

Claims 3 and 19 have been cancelled herein. The original language of Claim 3 has been included in Claim 1, as amended. Claim 19 was cancelled as being duplicative of Claim 23.

Claim 1 has been amended to recite a method for producing an improved particulate composition. Support for this amendment can be found throughout the Specification, for example, at page 24, lines 20-21 and in Claims 1 and 3 as originally filed. No new matter has been added.

Claims 4-8 have been amended. Claim 4, as amended, is now dependent on Claim 1 rather than Claim 3, which is cancelled herein. Support for this amendment can be found throughout the Specification and in Claims 4 as originally filed. Claims 5-8 have been amended to remove the term "targeted" from the claims. Support for this amendment can be found throughout the Specification and in the Claims as originally filed. No new matter has been added.

Rejection of Claims 3 and 4 Under 35 U.S.C. §112, second paragraph

Claims 3 and 4 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Examiner, it was unclear what exactly the limitation of Claim 3 was without any numbers or temperatures.

Claim 3 has been cancelled and Claim 4 has been amended to become dependent on Claim 1, thus the rejection is rendered moot. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-3, 5-10, 13-19, 22, 23 and 25-28 Under 35 U.S.C. §102(b)

Claims 1-3, 5-10, 13-19, 22, 23 and 25-28 are rejected under 35 U.S.C. §102(b) as being anticipated by Edwards *et al.* (U.S. Patent No: 5,985,309)("Edwards"). According to the Examiner, Edwards discloses a preparation of particles for inhalation. Specifically, Edwards discloses a method of spray drying insulin, which is combined with lactose and DPPC, and ethanol, with an inlet temperature of 110 degrees Celsius, and an outlet temperature of 61 degrees

Celsius; and wherein the resulting particles have a tap density of .05 and an aerodynamic diameter of 1.5 microns.

Applicants respectfully disagree. For anticipation under 35 U.S.C. §102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Edwards does not teach or suggest every aspect of the claimed invention.

Edwards teaches the advantages of aerodynamically light particles for drug delivery to the pulmonary system and the production of said particles. However, Edwards neither mentions the moisture content of the drying gas nor that the properties of the spray-dried particles can be controlled by manipulating the moisture content of the drying gas. Applicants teach that the moisture present in the drying gas can be optimized to produce particles which combine a large geometric diameter and a low tap density and which have aerodynamic properties that promote delivery to the lung. Thus Applicants teach that a correlation exists between the moisture content of the drying gas and the properties of the spray-dried particles which, if the optimal moisture content is selected, results in the formation of particles having desired properties.

Because Edwards does not teach every aspect of the claimed invention either explicitly or impliedly, Edwards does not anticipate the invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-6, 10-14, 16-20 and 22-28 Under 35 U.S.C. §102(a)

Claims 1-6, 10-14, 16-20 and 22-28 are rejected under 35 U.S.C. §102(a) as being anticipated by Bennett *et al.* (WO 01/00312) ("Bennett"). According to the Examiner, Bennett discloses a spray drying process for producing dry powder formulations for pulmonary delivery, and discloses the relative humidity of the drying zone.

Applicants respectfully disagree. For anticipation under 35 U.S.C. §102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Bennett does not teach or suggest every aspect of the claimed invention.

Bennett describes a system for producing dry powders wherein the system includes an atomizer and at least one conditioning zone coupled to the atomizer to suspend an atomized formulation for a residence time where the atomized formulation remains in the liquid state. (See page.4, lines 9-12) Bennett goes on to describe that as the atomized formulation passes through

at least one conditioning zone, the temperature and relative humidity are controlled to allow equilibration of the water activity, or water content, of the atomized droplet within the environment of the conditioning zone to promote amorphous to crystalline transformation of the formulation. (See page 5, lines 23-31) Thus, according to Bennett, a majority of the liquid phase is evaporated from the atomized formulation prior to the final drying process such that the droplets entering the conditioning zone leave as partially dried particles. These partially dried particles retain sufficient moisture to act as plasticizer and allow crystallization. (See page 14, lines 26-32) According to Bennett, this promotion of crystalline transformation leads to improved storage stability of the resulting dry powders. (See page 5, lines 10-11)

However, Bennett neither mentions the moisture content of the drying gas used to produce the spray-dried particles nor that the properties of the spray-dried particles can be controlled by manipulating the moisture content of the drying gas. Applicants teach that the moisture present in the drying gas can be optimized to produce particles which combine a large geometric diameter and a low tap density and which have aerodynamic properties that promote delivery to the lung. Thus Applicants teach that a correlation exists between the moisture content of the drying gas and the properties of the spray-dried particles which, if the optimal moisture content is selected, results in the formation of particles having desired properties.

Because Bennett does not teach every aspect of the claimed invention either explicitly or impliedly, Bennett does not anticipate the invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 2, 11 and 12 Under 35 U.S.C. §103(a)

Claims 2, 11 and 12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Edwards or Bennett in view of Broadhead et al. (Drug Development and Industrial Pharmacy, vol. 18, 1992)(“Broadhead”). According to the Examiner, Edwards does not teach the method of collecting the particles or using nitrogen, and Bennett does not teach nitrogen as the drying gas. However, the Examiner states that Broadhead teaches the use of a cyclone separator that collects the particles after drying, and that closed dryer systems also exist in which an inert gas like nitrogen can be used. Thus, according to the Examiner, it would have been obvious to one of

ordinary skill in the art at the time the invention was made to use nitrogen as the drying gas in Edwards or Bennett's method, if the composition required an organic feed medium.

Applicants respectfully disagree. Claims 2, 11 and 12 are dependent on Claim 1, and thus, assume all the limitations of Claim 1 with the further limitations that the drying-gas used in Claim 1 is selected from the group consisting of air, nitrogen, argon and any combination thereof; and that the resulting spray-dried particles are separated from the waste drying gas and are collected.

As discussed above, neither Edwards nor Bennett, alone or in combination, teach or suggest a method for producing an improved particulate composition as claimed by the Applicants. Thus, one of skill in the pertinent art, upon reading Edwards and Bennett, would not be motivated to modify the teachings therein to obtain the Applicants claimed invention.

Broadhead does not provide that which Edwards and Bennett lack. Broadhead neither mentions the moisture content of the drying gas used to produce the spray-dried particles nor that the properties of the spray-dried particles can be controlled by manipulating the moisture content of the drying gas. Therefore, Edwards, Bennett and/or Broadhead, alone or in combination, do not teach or suggest a method for producing an improved particulate composition as claimed by the Applicants. As such, the claimed invention is non-obvious over the prior art. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 10-14, 16-20 and 22-28 Under 35 U.S.C. §103(a)

Claims 10-14, 16-20 and 22-28 are rejected under 35 U.S.C. §103(a) as being unpatentable over Bennett *et al.* (WO 01/00312) ("Bennett"). According to the Examiner, Bennett discloses a spray drying process for producing dry powder formulations for pulmonary delivery, and discloses the relative humidity of the drying zone. Thus, according to the Examiner, it is deemed obvious to one of ordinary skill in the art to manipulate the conditions since Bennett teaches the general guidance and importance of reducing the final moisture content of the particles by controlling the temperature and humidity of the process.

Applicants respectfully disagree. As described above in response to the Examiner's 35 U.S.C. §102 rejection over Bennett, Bennett describes a system for producing dry powders wherein the atomized droplets are suspended for a residence time in a conditioning zone in which

the temperature and relative humidity are controlled to allow equilibration of the water content of the atomized formulation. Thus, according to Bennett, by controlling the water content of the atomized droplets prior to contact with the drying gas, amorphous to crystalline transformation of the atomized formulation is promoted leading to spray-dried particles having improved storage stability.

Bennett does not teach a system in which the moisture content of the drying gas is controlled to produce spray-dried particles having specific physical properties. Bennett describes the control of the moisture content of a different aspect of the spray-drying process (i.e., the atomized droplets rather than the drying gas as taught by Applicants), at a different point within the spray-drying process (i.e., in a conditioning zone prior to contacting the atomized droplets with the drying gas), for a different purpose (i.e., to promote amorphous to crystalline transformation rather than to produce spray-dried particles with specific physical properties). As such, one of skill in the art would not be motivated to use the teachings of Bennett to produce the Applicants claimed invention as there would be no reasonable expectation of success. Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-28 Under 35 U.S.C. §103(a)

Claims 1-28 are rejected under 35 U.S.C. §103(a) as being unpatentable over Edwards in combination with Bennett. According to the Examiner, Edwards discloses a preparation of particles for inhalation. Specifically, Edwards discloses a method of spray drying insulin, which is combined with lactose and DPPC, and ethanol, with an inlet temperature of 110 degrees Celsius, and an outlet temperature of 61 degrees Celsius; and wherein the resulting particles have a tap density of .05 and an aerodynamic diameter of 1.5 microns. Moreover, the Examiner states that Bennett discloses a spray drying process for producing dry powder formulations for pulmonary delivery, and discloses the relative humidity of the drying zone. Thus, according to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Edwards and Bennett since both teach a method of spray drying inhalation particles.

Applicants respectfully disagree. As discussed above, neither Edwards nor Bennett, alone or in combination, teach or suggest a method for producing an improved particulate composition

as claimed by the Applicants. Thus, one of skill in the pertinent art, upon reading Edwards and Bennett, would not be motivated to modify the teachings therein to obtain the Applicants claimed invention.

As such, the claimed invention is non-obvious over the prior art. Reconsideration and withdrawal of the rejection is respectfully requested.

Information Disclosure Statement

A Second Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Entry of the IDS is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Anne I. Craig

Anne I. Craig, Esq.

Registration No. 32,976

Telephone: (978) 341-0036

Facsimile: (978) 341-0136

Concord, MA 01742-9133

Dated: 12/19/02

MARKED UP VERSION OF AMENDMENTSClaim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A method for producing [spray dried particles having targeted aerodynamic properties comprising the steps of] an improved particulate composition comprising:
 - (a) controlling the moisture content of a drying gas, expressed as a dew point in degrees C, to a selected level which is maintained to an accuracy of at least 1 °C [selected to form spray dried particles having a targeted aerodynamic diameter or a targeted tap density];
 - (b) atomizing a liquid feed to form liquid droplets; and
 - (c) contacting the liquid droplets with the drying gas of step (a); [, thereby drying the liquid droplets to form spray dried particles having the targeted aerodynamic properties.]thereby drying the liquid droplets to form spray dried particles having the largest median geometric diameter, lowest median aerodynamic diameter, and a minimized tap density.
4. (Amended) The method of Claim 1 [claim 3] wherein the dew point is in the range between about 0° C and -40° C.
5. (Amended) The method of Claim 1 wherein the [targeted] aerodynamic diameter is less than about 5 microns.
6. (Amended) The method of Claim 5 wherein the [targeted] aerodynamic diameter is less than about 3 microns.
7. (Amended) The method of Claim [claim] 1 wherein the [targeted] tap density is less than about 0.4 g/cm³.
8. (Amended) The method of Claim 7 wherein the [targeted] tap density is less than about 0.1 g/cm³.